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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,962	05/30/2001	Olga Bandman	PF-0614-2 DIV	5425

27904 7590 12/15/2003

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	11

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,962	BANDMAN ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-81* is/are pending in the application.

4a) Of the above claim(s) *69,71,72,75,80 and 81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-68, 70, 73-74, 76-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 63-81 are pending. Claims 69, 71-72, 75, 80-81 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 63-68, 70, 73-74, 76-79 are under consideration.

Response to Amendment

Applicant's amendment and arguments filed 10/3/2003 have been fully considered but they are persuasive in part.

The objection to claims 63-65, 67-68, 70, 73-74, 76-79 as containing limitations drawn to non-elected subject matter has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claim 73 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues are set forth below.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 63-65, 67-68, 70, 73-74, 76-79 stand rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein, the protein encoded thereby, and an antibody to the encoded protein, for reasons of record set forth in Paper No. 10, 10/3/2003. The instant application does not disclose the biological role of this protein or its significance. The claimed invention is not supported by either a credible, specific and substantial asserted utility or a well-established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The rejection of record set forth that it is clear from the instant specification that the PKH-5 polypeptide has been assigned a function because of its similarity to known proteins (Specification at 73). Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the PKH-5 protein, therefore, there is no "real world" context of use for antibodies to the protein. Further research to identify or reasonably confirm a "real world" context of use is required.

Applicant argues that the protein to which the antibodies of the instant claims binds is a member of the protein kinase family by citing the reference of Nishigaki et al. which teaches a protein which is 51% identical to the protein of SEQ ID NO: 5. In the instant case, the filing date of the Application is 5/30/2001, with an effective filing date of 10/15/1998. The reference of Nishigaki et al. has a date of publication of April 11, 2003. Thus, this reference is post-filing, and as such, does not provide evidence that one of ordinary skill in the art would have

recognized that the identified specific and substantial utility was well-established at the time of filing. At the time of filing the function of the polypeptide of Nishigaki et al. was not known, nor were any specific disease associations known, and these references do not show that the PKH polypeptide had a well-established utility at the time of filing.

Applicant further argues that as demonstrated by the Furness Declaration (Dec. at ¶3), the person of ordinary skill in the art can achieve beneficial results from the claimed polypeptide is the absence of any knowledge as to the precise function of the protein. Brief at 7. The Furness Declaration argues that the claimed invention has specific, substantial, real-world utility by virtue of its use in toxicology testing, drug development and disease diagnosis through gene expression profiling. Brief at 10.

The question at issue is whether or not the broad general assertion that the claimed polypeptides might be used for some diagnostic application in the absence of a disclosure of which diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. The disclosure satisfies none of the three criteria See In re Kirk, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an Applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.")

First, Applicant argues, and cites the Furness Declaration (Dec. at ¶11, Brief at 11-12) as evidence, that toxicology testing is a well-established utility and concludes that the claimed polypeptides could be used in this manner and that the claimed invention possesses utility. Applicant further cites Rockett et al., Nuwaysir et al. and Steiner, as evidence that toxicology testing is now standard practice in the pharmaceutical industry. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case all nucleic acids and genes are in some combination useful in toxicology testing. However, the particulars of toxicology testing with SEQ ID NO: 5 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO: 5. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility that would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicant's individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to

perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polypeptide could be put.

With regard to drug discovery and development, (Dec. at ¶12) Applicant mentions expression profiling as one use of the claimed polypeptide in the instant application. Applicant states expression profiling is a method for identifying drug targets and characterize diseases. Such a profile is independent of the function of the genes or gene products. In the instant case, the claimed polypeptide can be used as one of many targets on a microarray to generate an expression profile. A transcript image thus generated from lung tumor tissue can be compared, for example, with that from lung tumor tissue treated with a potential therapeutic compound in order to evaluate the efficacy of the compound.

However, there is no way to assess the meaning of any individual hit obtained from this procedure. The first requirement is that one must know the biological significance of the polypeptide which is being evaluated. Without this information, the results of the expression profile is useless because one would not know if the polypeptide expression should be increased or decreased or even what significance could be attributed to such changes in expression profiles.

Applicant further argues, citing the Furness Declaration (Brief at 8, Dec. at ¶9) the utility of the claimed polypeptide in the diagnosis of disease. However, in order for a polypeptide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polypeptide and the

disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polypeptide and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing. Brenner, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. § 101.

The Furness Declaration argues (Dec. at ¶10) that selectivity screening is a well-established utility and concludes that the claimed polypeptides could be used in this manner and that the claimed invention possesses utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case all nucleic acids and genes are in some combination useful in selectivity screening. However, the particulars of selectivity screening with SEQ ID NO: 5 are not disclosed in the instant specification. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO: 5. Because of

this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in an array for selectivity screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicant's individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polypeptide could be put.

Applicants assert the databases sold by Applicants' assignee, Incyte, include exactly the kinds of information made possible by the claimed invention, such as tissue and disease associations, Incyte sells its database containing the cloned sequence and millions of other sequences throughout the scientific community, including to pharmaceutical companies who use the information to develop new pharmaceuticals. Brief at 13.

However, this assertion fails to address the utility of the individually claimed polypeptide of the invention of the instant application. The claims are to isolated polypeptides, not to descriptive information included in a database. The commercial success of a database containing the sequence information of the claimed polypeptide does not confer a specific and substantial

utility to the individual polypeptide as one of skill in the art would need to conduct further experimentation to determine the use of the individual member of the database.

The previous Office Action further set forth that even if, *arguendo*, a patentable utility is found for antibodies to the PKH-5 protein, claims 63-65, 67-68, 70, 73-74, 76-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for an antibody which binds to a polypeptide comprising a naturally occurring amino acids sequence which is 90% identical to SEQ ID NO: 5, or for an antibody which binds to a polypeptide comprising an immunogenic fragment of SEQ ID NO: 5, for reasons of record set forth in Paper No. 10, 10/3/2003. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide enablement for an antibody which binds to a polypeptide comprising a naturally occurring amino acids sequence which is 90% identical to SEQ ID NO: 5, or for an antibody which binds to a polypeptide comprising an immunogenic fragment of SEQ ID NO: 5. Claims 63-65, 67-68, 70, 73-74, 76-79 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides to which the antibodies are directed will retain the characteristics of PKH-5 activity. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

Applicant argues that claim 1 recites not only that the variant polypeptides have at least 90% sequence identity to SEQ ID NO: 5, but also have "a naturally occurring amino acid

sequence." Through the process of natural selection, nature will have determined the appropriate amino acid sequences. Thus, one skilled in the art need not make and test vast numbers of polypeptides that are based on the amino acid sequence of SEQ ID NO: 5. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature. Brief at 22.

The specification provides adequate guidance for making SEQ ID NO: 5 however the specification fails to provide guidance on use of this polypeptide sequence. As set forth in In re Fisher, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

The unpredictability of the protein art is demonstrated in Voet (supra), which shows the large effect that even a single amino acid change can have on protein structure and function. This is a demonstration of the unpredictability of the protein art when trying to predict the function of a protein given only the primary amino acid sequence.

In Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic

sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case there are a large number of polypeptide sequences which have 90% sequence identity to SEQ ID NO: 5 and are naturally occurring, however these sequences are various unrelated proteins, and no function is disclosed for the polypeptides encompassed by the claims. Therefore, while the specification provides the necessary guidance to make the polypeptide set forth in SEQ ID NO: 5 or polypeptide sequences which are 90% identical to SEQ ID NO: 5, it does not provide the necessary guidance for one of skill in the art to use the polypeptide sequence of SEQ ID NO: 5, or polypeptide sequences which are 90% identical to SEQ ID NO: 5. Further, since no function is associated with the PKH protein encoded by SEQ ID NO: 5, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time the invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.

Claims 63-65, 67-68, 70, 73-74, 76-79 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No. 10, 10/3/2003. Applicant is directed to the Guidelines for the Examination of Patent

Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to an antibody which binds to a polypeptide comprising a naturally occurring amino acids sequence which is 90% identical to SDEQ ID NO: 5. The claims also encompass an antibody that binds to a polypeptide comprising an immunogenic fragment of SEQ ID NO: 5. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The claims encompass antibodies directed to variant polypeptides, and fragments of polypeptides, and the art recognizes the unpredictability of the effect of mutations on protein function. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of antibodies to polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from

the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the antibodies to polypeptides encompassed: there is no guidance in the art as to what the defining characteristics of the polypeptides might be. Thus, no identifying characteristics or properties of the instant antibodies are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim 63 sets forth the limitation that the claimed antibody must be directed to naturally occurring amino acid sequence which having protein kinase activity. However, in University of California v. Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. the Court decided that a definition by function alone "does not suffice" to sufficiently describe a biomolecule "because it is only an indication of what the gene does, rather than what it is." Further, "it is only a definition of a useful result rather that a definition of what achieves that result...The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention". *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111,

clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

The application on page 16, lines 20-34 sets forth a method of obtaining a PKH-5, variant or derivative that retains protein kinase activity. However, in Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016 at 1022 it was held that "when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e. until after the gene has been isolated". While Applicant has set forth a method for obtaining a PKH-5 naturally occurring variant which retains protein kinase activity, Applicant has not set forth within the claim the detailed constitution of the PKH-5 naturally occurring variant which retains protein kinase activity, and thus does not satisfy the written description requirement.

Applicant argues that one of ordinary skill in the art would recognize polypeptide sequences which are variants having at least 90% amino acid sequence identity to SEQ ID NO: 5. Given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art recognize whether it was a variant of SEQ ID NO:5, and that the subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO: 5. Brief at 25.

The instant claims are drawn to the polypeptide sequence of SEQ ID NO: 5, or polypeptide sequences which are 90% identical to SEQ ID NO: 5. The written description

requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Considering all disclosed distinguishing identifying characteristics such as:

A: Partial structure - Only the structure of SEQ ID NO: 1 has been provided.

B: Physical and/or chemical properties - Only the physical or chemical properties of SEQ ID NO: 1 are provided.

C: Functional characteristics - The claimed the polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1 does not have a disclosed function, as set forth supra.

D: Known or disclosed correlation between structure and function - No structural/functional relationship is disclosed for the claimed polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1.

E: Method of making - Methods of making are disclosed.

F: Combinations of A-E - No combination of the other factors will adequately describe the claimed antagonist.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the

genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The specification does not describe sequences which have a biological function for any sequence 90% identical to SEQ ID NO: 1. Because the specification fails to describe more than a single species of each genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met. The specification provides a written description only for PKH which is encoded by nucleic acids set forth in SEQ ID NO: 1.

Thus, in weighing all the factors in view of the level of skill and the knowledge in the art and in light of and consistent with the written description, one of skill in the art would recognize from the disclosure that Applicant was not in possession of the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63-65, 67-68, 70, 73-74, 76-79 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention, for reasons of record set forth in Paper No. 10, 10/3/2003.

Claims 63 and 65 are indefinite in the recitation of the term "naturally occurring". It is unclear whether this term imposes a required limitation on the claim, such that it only encompasses, for example, polynucleotides amplified from human cDNA, or only sequences produced by digestion with restriction enzymes of DNA isolated from tissue which contains polynucleotides encoding the polypeptide, or if the claim encompasses all polynucleotide sequences that encode the polypeptide. Therefore, the metes and bounds of the claim are unclear. Claims 64, 67-68, 70, 73-74, 76-79 are rejected due to their dependence on claims 63 and 65.

Applicant argues that the use of the term "naturally-occurring" defines where to find the amino acid sequence encompassed by the claims. However, in reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph "by providing clear warning to others as to what constitutes infringement of the patent". See MPEP 2173.02, MPEP 2173.02. In the instant case, Applicant's argument that the use of the term "naturally-occurring" only refers to where to find the amino acid sequence encompassed by the claims could conceivably lead to the situation where identical polypeptides would or would not be infringing depending on whether they were isolated from natural sources, or only derived from a natural protein but produced synthetically. This would not provide clear warning of infringement.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 4, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600